


And eosinophilia after a stay in the tropics ?


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Joint Symposium with the Scientific Study Group for Travel medicine




Should we investigate ?

- Diagnosis of tropical conditions causing eosinophilia is important:
 - Almost all helminths can occasionally cause serious pathology
 - Almost all helminths are easily treated
- Untargeted investigation can be
 - Time consuming
 - Frustrating for physician & patient
 - Expensive



Should we investigate ?

- Wide variety of causes:
 - Allergic illness
 - Skin diseases
 - Malignant conditions
 - Hematological disorders
 - Medication use
 - Parasitic infection
 - ...



Rothenberg ME. Eosinophilia. *N Engl J Med*. 1998;338:1592-600

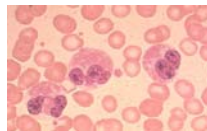
How to investigate ?

- Identifying / ruling out as many important diagnoses on the 1st occasion
- Taking account of the prevalence of helminth infections in area of travel



How to define eosinophilia

- Normal subjects < 350/mL (1-3%)
- Daytime fluctuation (cortisol) up to 40%
- Absolute more reliable than percentage
- Degree of eosinophilia:
 - Mild : up to 1500/mL
 - Moderate: 1500-5000/mL
 - Severe > 5000/mL



Nutman TB. Evaluation and differential diagnosis of marked, persistent eosinophilia. *Immunol Allergy Clin North Am* 2007; 27:329-69

Common finding ?

- 5% of travellers returning from tropics?
- 8%-10% in asymptomatic returning travellers
- Related to destination:
 - 48% from Africa vs 31% of all destinations
 - highest RR 2,95 for West- and central-Africa
 - Lowest RR for Indian subcontinent and Latin America

Schlyte C. Diagnostic significance of blood eosinophilia in returning travelers. *Clin Infect Dis* 2002;34:407-11
Whitty CJ. Utility of history, examination and laboratory tests in screening those returning to Europe from the tropics for parasitic infection. *Trop Med Int Health* 2000;5:818-23
Lloman MD. Screening for schistosomiasis, filariasis and strongyloidiasis among expatriates returning from tropics. *Clin Infect Dis* 1995;17:353-9

Eosinophilia ≠ helminth

- 36% definite diagnosis (19% helminth)
- PPV 14% for helminth infection
- Up to 39% ?
- Diagnostic value of eosinophilia alone is limited

Schulte C. Diagnostic significance of blood eosinophilia in returning travelers. *Clin Inf Dis* 2002;34:407-11
Libman MD. Screening for schistosomiasis, filariasis and strongyloidosis among expatriates returning from tropics. *Clin Infect Dis* 1993;17:353-9
Harris et al. Eosinophilia in Caucasians returning from the tropics. *Trans R Soc Trop Med Hyg* 1986;80:327-8

Symptoms

- Asymptomatic 21-30%
- Gastro-intestinal symptoms 27%
- Skin related symptoms 15%
- Fatigue, non-specific symptoms 37%
- Difference between traveller & immigrant:
- Up to 80% have asymptomatic intestinal helminths

Schulte C. Diagnostic significance of blood eosinophilia in returning travelers. *Clin Inf Dis* 2002;34:407-11
Wetham J. Investigation of tropical eosinophilia. assessing a strategy based on geographical area. *J Infect* 2003;46:180-5

Travel history



- "Unde venis? "
- When did you travel, how long, when did you return?
- What did you do ?
- Exposure:
 - Drinking untreated water / unpasteurised milk
 - Undercooked fish or meat
 - 'Fresh water' swimming
 - Bare foot walking
 - Contact with locals?
- Symptoms in other travellers ?

UCL

Timing

- Eosinophilia may be transient
 - Tissue migration phase
 - Prepatent period: no ova detectable
- Serological tests: 4-12 weeks after infection
 - Sometimes cross-reaction between tests



Investigating asymptomatic eosinophilia

- Common causes: intestinal helminths, schistosomiasis, strongyloides and filaria
- All travellers : (concentrated) stool examination, *strongyloides* serology
- Returning from Africa: + serology schisto and filaria, and urine analysis for ova *Schistosoma haematobium*
- Returning from West Africa: + serology filaria, (day-night) blood exam for filaria, skin snips (sero+)



Wetham J. Investigation of tropical eosinophilia: assessing a strategy based on geographical area. *J Infect* 2003;46: 180-5




Investigating asymptomatic eosinophilia



Checkley A. et al. Eosinophilia in returning travellers and migrants from the tropics: UK recommendations for investigation and initial management. *J Infect* 2010;60:1-20



Eosinophilia with symptoms

Fever	GI symptoms	Skin	Other
<ul style="list-style-type: none"> • Katayama • Loeffler • Visceral larva migrans • Tropical pulmonary eosinophilia 	<ul style="list-style-type: none"> • Ascariasis • Strongyloidiasis • Bilharzia • <i>Trichuris T.</i> • <i>Trichinella sp.</i> • Anisakiasis • Fascioliasis • ... 	<ul style="list-style-type: none"> • Filariasis • Gnatostomiasis • Larva migrans • Larva currens 	<ul style="list-style-type: none"> • Paragonimiasis • <i>S. Haematobium</i>

Eosinophilia with fever


- Katayama fever – *Schistosoma sp.*
 - Incubation 2-9 weeks
 - Africa
 - Fresh water exposure: cercaria penetrate skin
 - severe eosinophilia, fever, dry cough, urticarial rash
 - Low sensitivity of stool/urine exam and serology
 - Corticosteroids + praziquantel 40 mg/kg (repeat)

Botteau E et al. Imported Katayama fever: clinical and biological features at presentation and during treatment. *J Infect* 2006;32: 338-45

Eosinophilia with fever

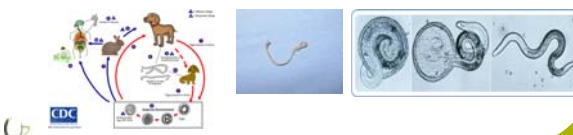
- Loeffler's syndrome:
 - Migration of larval stadia of nematodes
 - *Ascaris L.*, strongyloides, hookworms
 - Incubation 1-2 weeks
 - Fever, urticaria, wheezes, dry cough
 - Clinical diagnosis, migratory infiltrates on XR
 - Charcot-Leyden crystal
 - Albendazole 400 mg bd 3days



Cheddey A et al. Eosinophilia in returning travellers and migrants from the tropics: UK recommendations for investigation and initial management. *J Infect* 2010;60:1-20

Eosinophilia with fever


- **Visceral larva migrans – acute toxocariasis**
 - worldwide
 - Ingestion soil contaminated eggs *T.Canis T.catis*
 - Mostly children
 - Often asymptomatic, fever, wheezes, cough
 - Abdominal pain, HSM, urticarial rash
 - Serology
 - Albendazole 400 mg, steroids, antihistamine



Despommier D. Toxocariasis: clinical aspects, epidemiology, medical ecology, and molecular aspects. Clin Microbiol Rev. 2003;16:265-72.

Eosinophilia with fever


- **Tropical pulmonary eosinophilia – *W.Bancrofti* / *B. Malayi***
 - Hypersensitivity reaction < lymphatic filarial worms
 - Fever, dry cough, dyspnea, wheezes
 - Severe eosinophilia, IgE, chest XR, PFT
 - Serology +, blood microscopy –
 - DiEthylCarbamazine ± steroids
 - Delayed or incomplete treatment : lymphatic damage and fibrosis



Boogild AK et al. Tropical pulmonary eosinophilia: a case series in a setting of nonendemicity. Clin Infect Dis 2004;39:1123-8

Eosinophilia with GI-symptoms


- **Ascariasis – *Ascaris lumbricoides***
 - World-wide , faeco-oral transmission
 - Pre-patent period 2-3 months
 - May present acutely: Loeffler's syndrome
 - Asymptomatic, vague abdominal pain, diarrhea
 - Obstruction (children), biliary obstruction
 - Concentrated stool exam
 - Albendazole 400 mg once (or mebendazole 100mg bd 3days)



Kester J et al. Efficacy of current drugs against soil transmitted helminth infections: systematic review and meta-analysis. J Am Med Assoc 2008;299:1937-48

Eosinophilia with GI-symptoms

- Strongyloidiasis - *Strongyloides stercoralis*
- Incubation period: days to weeks for larva currents (or Loeffler's syndrome), 2 weeks later vague abdominal symptoms (diarrhea, bloating)
- Serology ! Low sensitivity of stool samples
- Ivermectin 200µg/kg once
- Hyperinfestation syndrome:
 - Paralytic ileus , G-sepsis (<translocation across bowel wall)
 - Often pulmonary involvement (larva ++ sputum and stools)
 - Low or absence of eosinophilia !
 - Associated with steroids, chemo/malignancy, HTLV-1
 - Broad-spectrum AB, ivermectin IV (duration?)



Chiodini PL et al. Parenteral ivermectin in Strongyloides hyperinfection. Lancet 2000 Jan 1;355(9197):43-41

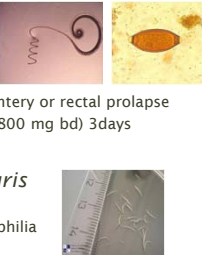
Eosinophilia with GI-symptoms

- Bilharzia – *Schistosoma mansoni (japonicum)*
- *S.Mansoni*: Africa, Arabian peninsula, S-America
- *S.Japonicum*: China, Indonesia, Phillipines
- Swimmer's itch , Katayama fever
- Abdominal pain, diarrhea (heavy infection, dysentery)
- Serology (4-8 wks), stool exam (low sensitivity)
- Praziquantel 40mg/kg single dose
- Chronic infection: HSM, fibrosis, portal HT , esophageal varices (endoscopy, ultrasound)



Eosinophilia with GI-symptoms

- Whipworm - *Trichuris trichiura*
- Worldwide, faeco-oral transmission
- Prepatent period: 4-12 weeks
- Usually asymptomatic
- Heavy infestation in children: anemia, dysentery or rectal prolapse
- Mebendazole 100mg bd (albendazole 400-800 mg bd) 3days
- Pin worm – *Enterobius vermicularis*
- Worldwide, faeco-oral transmission
- Pruritis ani, occasionally colitis with eosinophilia
- "sellotape test"
- Albendazole 400 mg (mebendazole 100 mg) single dose



Eosinophilia with GI-symptoms




- **Trichinellosis – *Trichinella sp.*** 
- Consumption of raw (undercooked) meat; outbreaks
- Worldwide (Eastern Europe, Russia, Argentina, China)
- Incubation: 7-30 days (enteral phase), 2-6 weeks (parenteral)
- Enteral phase: abdominal pain, N+V+D+, fever
- Parenteral phase: myalgia, weakness.
 - Respiratory failure, facial/periorbital edema, conjunctivitis, rash
 - Severe presentation : meningo-encephalitis, myocarditis
- Creatinine kinase levels ↑, severe eosinophilia
- Serology , muscle biopsy
- Albendazole 400 mg 3 days
- 14 days severe disease (with prednisolone)



Watt G et al. Blinded, placebo controlled trial of antiparasitic drugs for trichinosis myositis. J infect Dis 2000;182:371-4
Shimon et al. The use of prednisone in the treatment of trichinellosis. Br med Assoc J 2007;9:937-9


Eosinophilia with GI-symptoms

- **Anisakiasis – *Anisakis spp.***
- Worldwide (consumption raw/pickled seafood)
- Incubation 2-5 hours
- Acute severe abdominal pain, N+V+
- Rarely anaphylaxis
- Diagnosis usually at endoscopy, serology
- Endoscopic (surgical) removal (or albendazol 400 mg)

Moore DA et al. Treatment of anisakiasis with albendazole. Lancet 2002;360:54


Eosinophilia with GI-symptoms

- ***Fasciola hepatica / F. gigantica*** 
- Worldwide (Middle East, SE Asia, Eastern Europe)
- Consumption of contaminated vegetation (intermediate encysted metacercaria) eg. watercress
- Incubation 3-12 weeks, prepatent period 3-4 months
- Acute phase: (month 3-5) fever, hepatomegaly with pain
- Chronic phase: biliary obstruction, cholecystitis, abscess (50% asymptomatic)
- Diagnosis:
 - Acute phase : clinical, serology confirms later.
 - Chronic phase: serology, (stool microscopy), imaging (US or CT)
- Triclabendazole 10 mg/kg single dose

Hien TT et al. A randomized controlled pilot study of artesunate versus triclabendazole for human fascioliasis in central Vietnam. Am J Trop med Hyg 2008;78:388-92

Eosinophilia with GI-symptoms


- Other causes:
 - Protozoa: *Isospora bella*, *Dientamoeba fragilis*, Toxoplasmosis
 - Tapeworm: *Taenia saginata* / *T.Solium* (cysticercosis)
 - Dwarf tapeworm: *Hymenolepis nana*
 - Hookworms: *Ankylostoma braziliensis*, *Necator americanus*
 - Hydatid disease: *Echinococcus granulosus*, *E. multilocularis*
 - *Angiostrongylus costaricensis*
 - Liver flukes: *clonorchis sinensis*, *Opisthorchis* sp.
 - ...



Eosinophilia with skin/musculoskeletal symptoms

- Cutaneous larva migrans
 - Characteristic migratory rash
 - Ivermectin 200 µg/kg (or albendazole 400 mg od 3 days)
- Larva currens – *Strongyloides stercoralis*
 - Itchy, linear, urticarial rash
 - Usually trunk, upper legs, and buttocks
- Trichinellosis – *Trichinella spiralis*
 - 2nd 'parenteral' phase: facial, periorbital edema, urticarial rash myalgia
- Schistosomiasis: 'swimmer's itch'
 - Itchy maculo-papular rash
 - Often caused by *schistosoma* spp. of birds







Eosinophilia with skin/musculoskeletal symptoms

- Onchocerciasis – *onchocerca volvulus*
 - Near rivers, predominantly Africa
 - Incubation 8-20 months
 - Diffuse pruritic dermatitis (legs and buttocks)
 - 'leopard skin' in chronic cases
 - Anterior chamber eye: keratitis, uveitis, choroidoretinitis
 - Serology; skin snips, slip lamp exam
 - Ivermectin 200 µg/kg repeated for months

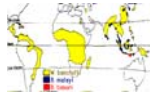





McCarthy JS et al. Onchocerciasis in endemic and nonendemic populations: differences in clinical presentation and immunologic findings. *J Infect Dis* 1994;170:736-41

Eosinophilia with skin/musculoskeletal symptoms



- Lymphatic filariasis - *W.bancrofti*, *B. malayi*
 - incubation period: 1 to 16 months
 - *W.bancrofti*: worldwide tropical, *B. malayi*: mainly Asia
 - Fever, lymphadenitis, lymphoedema
 - Non-immune travellers: fever, respiratory symptoms
 - Serology, microscopy 'night' blood (midnight)
 - DiEthylCarbamazine, limb care

UCL
Ottesen EA Lymphatic filariasis: treatment, control and elimination. Adv Parasitol 2006;61:395-441

Eosinophilia with skin/musculoskeletal symptoms

- Loiasis - *Loa Loa*
 - Incubation 6 months to 6 years
 - West and Central Africa
- Migratory 'calabar' soft tissue swelling of limbs
- 10-20% cases: migrating worm across conjunctiva
- Serology, 'day' blood microscopy
- DiEthylCarbamazine

UCL
Nutman TB, et al. Loa Loa infection in temporary residents of endemic regions: recognition of a hyperresponsive syndrome with characteristic clinical manifestations. J Infect Dis 1986; 154: 110-8

Eosinophilia with skin/musculoskeletal symptoms

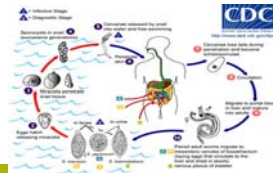
- Gnathostomiasis - *Gnathostoma spinigerum*
 - Incubation only 3-7 days
 - SE Asia, usually outbreaks
 - Eating undercooked fish, chicken (frog, snake)
 - Intermittent subcutaneous swelling, pruritus
 - Occasionally eosinophilic meningitis, myelitis
 - Clinical diagnosis, serology
 - Albendazole 400 mg bd 3 weeks




UCL
Nontasart P et al. Comparison of ivermectin and albendazole treatment for gnathostomiasis. Southeast Asian J Trop Med Public Health 2000 Jun; 31(2):374-7

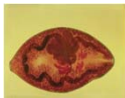
Eosinophilia with urinary symptoms

- **Bilharzia – *Schistosoma haematobium***
 - Africa (great lakes, Malawi, Victoria, Okavango)
 - Hematuria (micro/macro), dysuria, hematospermia
 - Serology , urine analysis
 - Praziquantel 40 mg/kg once
- Long term complications: squamous cell bladder Ca, obstructive uropathy



Eosinophilia with pulmonary symptoms

- **Paragonimiasis – *Paragonimus sp.***
 - Most cases SE Asia
 - Ingestion raw crab or crayfish
 - Abdominal pain, diarrhea, urticaria
 - Pleuritic chest pain, pleural effusions, chronic cough, hemoptysis
 - Chest XR, Sputum analysis, serology
 - Praziquantel 25 mg tds (2days)



Take home messages

- Eosinophilia is common in returning travellers
- Always investigate eosinophilia in a returning traveller
- Wide variety of causes
- Diagnostic value of eosinophilia alone has limited value



Take home messages

- About 1/3 asymptomatic
- Degree of eosinophilia
- Travel history !



Take home messages

- In all travellers stool exam, *strongyloides* serology
- Africa: include schisto/filarial serology
- West & Central Africa
 - Also include blood exam for microfilaria
- Investigate
 - Symptoms
 - Region of travel and prevalence of helminths